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(FILE 'HOME' ENTERED AT 08:30:58 ON 18 DEC 2003)

FILE 'DISSABS, IMOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
COMPUAB, CONF, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, LIFESCI, OCEAN,
MEDICONF, PASCAL, PAPERCHEM2, POLLUAB, SOLIDSTATE, ADISCTI, ADISINSIGHT,
ADISNEWS, ANABSTR, BIOBUSINESS, BIOCOMMERCE, ...' ENTERED AT 08:31:33 ON
18 DEC 2003

	E MAYO STEPHEN?/AU
L1	11 S E1 OR E2 OR E4
	E SHIFMAN JULIA?/AU
L2	16 S E1 OR E2 OR E4
	E SHIMAOKA MOTOMU?/AU
L3	84 S E1 OR E2
	E SPRINGER TIMOTHY?/AU
	E SPRINGER?/AU
L4	1827 S ((BIASED OR OPEN OR CLOSE OR CONFORMATION) (S) (I (A) DOMAIN))
L5	30 S L4 AND(L1 OR L2 OR L3)
L6	13 DUP REM L5 (17 DUPLICATES REMOVED)
L7	77 S L4 (S) (ALPHA (A) M)
L8	14 S L7 (S) (139 OR 153 OR 156 OR 157 OR 160 OR 199 OR 215 OR 21
L9	11 DUP REM L8 (3 DUPLICATES REMOVED)

FILE 'DISSABS, IMOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
COMPUAB, CONF, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, LIFESCI, OCEAN,
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FILE 'DISSABS, IMOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
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18 DEC 2003

L6 ANSWER 13 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11

ACCESSION NUMBER: 2000:451152 BIOSIS

DOCUMENT NUMBER: PREV200000451152

TITLE: Computational design of an integrin I
domain stabilized in the **open** high
affinity **conformation**.

AUTHOR(S): **Shimaoka, Motomu; Shifman, Julia M.**;
Jing, Hua; Takagi, Junichi; Mayo, Stephen L. [Reprint
author]; Springer, Timothy A.

CORPORATE SOURCE: Howard Hughes Medical Institute and Division of Biology,
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SOURCE: Nature Structural Biology, (August, 2000) Vol. 7, No. 8,
pp. 674-678. print.
ISSN: 1072-8368.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Oct 2000

Last Updated on STN: 10 Jan 2002

AB We have taken a computational approach to design mutations that stabilize
a large protein domain of apprxx200 residues in two alternative
conformations. Mutations in the hydrophobic core of the alphaMbeta2
integrin I **domain** were designed to stabilize the
crystallographically defined **open** or closed conformers. When
expressed on the cell surface as part of the intact heterodimeric
receptor, binding of the designed **open** and closed I
domains to the ligand iC3b, a form of the complement component C3,
was either increased or decreased, respectively, compared to wild type.
Moreover, when expressed in isolation from other integrin domains using an
artificial transmembrane domain, designed **open** I
domains were active in ligand binding, whereas designed closed and
wild type I **domains** were inactive. Comparison to a
human expert designed open mutant showed that the computationally designed
mutants are far more active. Thus, computational design can be used to
stabilize a molecule in a desired **conformation**, and
conformational change in the I **domain** is
physiologically relevant to regulation of ligand binding.